REMARKS

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks and accompanying information, which place the application in condition for allowance.

1. Status Of Claims And Formal Matters

The specification has been amended to add sequence identifiers. No new matter has been added.

Claims 1-4, 11, 16, 22-23, 26-29 are under consideration in this application. Claims 1 and 16 have been amended, claims 26-29 are cancelled, and claims 31 and 32 have been added. No new matter has been added by this amendment.

Support for the recitation of a tripeptide is inserted into a homogeneous serotype fiber may be found on page 49, lines 4-20. Support for the recitation of introducing an adenovirus to primary tumor cells *in* vitro or *ex vivo* may be found on page 28, lines 17-18. Support for the recitation of an Ad5 adenovirus and an Ad5 fiber knob is found on page 49, lines 4-20. No new matter has been added.

The Examiner is thanked for withdrawing the previous rejection of claims 1-4, 9, 11, 16 and 23 under 35 U.S.C. § 112, first paragraph and the previous rejection of claims 1-4, 9, 11, 16 and 22-25 under 35 U.S.C. § 112, second paragraph. The Examiner is also thanked for withdrawing the objection of the specification. The Examiner is further thanked for withdrawing the rejection of claims 16 and 22-23 under 35 U.S.C. § 103(a).

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

2. The Rejections Under 35 U.S.C. § 112, First Paragraph, Are Overcome

Claims 1-4, 9, 11, 16, 22, 23 and 26-29 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Claims 26-29 have been cancelled, thereby obviating the rejection, in part.

Claims 1 and 16 have been clarified to recite a recombinant adenovirus that mediates enhanced gene transfer to primary tumor cells, wherein said adenovirus comprises a modified fiber comprising a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob, wherein the tripeptide is inserted into a homogeneous serotype fiber, thereby obviating the rejection. Support for the recitation of a tripeptide is inserted into a homogeneous serotype fiber may be found on page 49, lines 4-20. Since claims 2-4, 9 and 11 depend from claim 1, and claims 22 and 23 depend from claim 16, the rejection to claims 2-4, 9, 11 and claims 22 and 23 have also been obviated.

It is believed that the rejections under 35 U.S.C. § 112, first paragraph, have been overcome. Reconsideration and withdrawal are respectfully requested.

3. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Are Overcome

Claims 16, 22, 23, 27 and 29 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner alleges that claim 16 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein.

Claims 27 and 29 have been cancelled, thereby obviating the rejection, in part.

As suggested by the Examiner, claim 16 has been clarified to include a recitation of introducing the adenovirus to primary tumor cells *in vitro* or *ex vivo*, thereby obviating the rejection. Since claims 22 and 23 depend from claim 16, the rejection to claims 22 and 23 has also been obviated. Claims 24 and 25 have been canceled.

It is believed that the rejections under 35 U.S.C. § 112, second paragraph, have been overcome. Reconsideration and withdrawal are requested.

4. The Rejections Under 35 U.S.C. § 102(e) Are Overcome

Claims 1-4, 9 and 11 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Wickham *et al.* (U.S. Patent No. 5,846,782, hereinafter "the '782 patent"). The Examiner contends that the '782 patent anticipates the claimed invention because the '782 patent teaches modification in the HI loop, including insertion of RGD peptide, and gene transfer in tumor cells. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein. The cited reference does not anticipate the instant invention.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, the reference relied upon by the Office Action does not disclose, suggest or enable Applicants' invention. Claim 1 has been clarified to recite a recombinant adenovirus that mediates enhanced gene transfer to primary tumor cells, wherein said adenovirus comprises a modified fiber comprising a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob, wherein the tripeptide is inserted into a homogeneous serotype fiber.

The '782 patent relates to the use of an adenovirus 5 (Ad5) serotype vector wherein the ligands are inserted into the HI loop of an Ad2 serotype vector, thereby providing an Ad5/Ad2 fiber chimera, with the ligand surrounding sequences derived from Ad2 (see, e.g., Example 1 of the '782 patent, column 21, lines 31 to 43). Accordingly, the '782 patent does not teach or suggest the insertion of any ligand into a homogeneous serotype fiber.

Applicants submit that it is widely accepted in the art that changes made by mutations, deletions and insertions into peptide sequences will have a wide variety of effects depending on the surrounding sequences. For example, the '782 patent asserts that there is a 100 fold binding difference between an RGD sequence with or without surrounding cysteine amino acids (see, e.g., Example 6 of the '782 patent, column 30, lines 19 to 26). Accordingly, there is a distinct difference between inserting an RGD sequence into a homogeneous serotype fiber of the present invention and the chimeric fiber of the '782 patent.

Consequently, reconsideration and withdrawal of the Section 102 rejections are earnestly requested.

5. The Rejections Under 35 U.S.C. §103 Are Overcome

Claims 1, 4 and 28 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wickham *et al.* (WO 96/26281, hereinafter "the '281 publication") taken with the '782

patent. The Examiner alleges that the '281 publication teaches incorporating a non-native binding domain (RGD) peptide within an exposed loop of a mutant adenovirus to create a fiber chimera and producing recombinant adenovirus comprising the fiber chimera, but the '281 publication does not specifically teach that the exposed loop of the adenovirus is the HI loop of the fiber knob. The Examiner further contends that the '782 patent teaches producing adenoviruses comprising a modified fiber protein contain an RGD motif and that the exposed loop is preferably the HI loop of the fiber knob. This rejection is respectfully traversed. This rejection is moot in light of the amendments to the claims submitted herein. The cited reference does not make the instant invention obvious.

Claim 28 has been cancelled, thereby obviating the rejection, in part.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Applying the law to the instant facts, the reference relied upon by the Office Action does not disclose, suggest or enable Applicants' invention. Claim 1 has been clarified to recite a recombinant adenovirus that mediates enhanced gene transfer to primary tumor cells, wherein said adenovirus comprises a modified fiber comprising a tripeptide having the sequence Arg-Gly-Asp (RGD) into the HI loop domain of the fiber knob, wherein the tripeptide is inserted into a homogeneous serotype fiber.

The '281 publication does not teach or suggest inserting any ligand, let alone an RGD peptide, into a homogeneous serotype fiber. In fact, Examples 3 and 5 of the '281 publication relate to inserting an RGD sequence into chimeric, i.e., heterogeneous, serotype fibers. For example, Example 3 relates to a mouse adenovirus type 1 and Ad5 fiber chimera (see, e.g., page 24, line 16 to page 25, line 6 of the '281 publication). Similarly, Example 5 relates to an

Ad2/Ad5 fiber chimera (see, e.g., page 26, line 18 to page 27, line 20 of the '281 publication). Accordingly, there is no teaching or suggestion in the '281 publication to insert an RGD sequence into a homogeneous serotype fiber. As discussed above, the '782 patent does not teach or suggest inserting an RGD sequence into a homogeneous serotype fiber.

Consequently, reconsideration and withdrawal of the Section 103 rejections are earnestly requested.

6. The Double Patenting Rejections Are Overcome

Claims 1, 2, 4, 9, 11 and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 2 and 12 of U.S. Patent No. 6,824,771 ("the '771 patent").

Claim 28 has been cancelled, thereby obviating the rejection, in part.

The issue of whether there is indeed double patenting is contingent upon whether the remarks herewith are indeed considered and entered; and, if so, whether the Examiner believes there is overlap with claims ultimately allowed in the application. If, upon agreement as to allowable subject matter, it is believed that there is still a double patenting issue, a Terminal Disclaimer as to the '771 patent will be filed for the purposes of expediting prosecution.

Accordingly, reconsideration and withdrawal of the double patenting rejection, or at least holding it in abeyance until agreement is reached as to allowable subject matter, is respectfully requested.

Claims 1, 2, 4, 9, 11 and 28 are allegedly directed to an invention not patentably distinct from claims 1, 2 and 12 of the '771 patent. Applicants respectfully submit that the '771 and the present application are commonly owned by The UAB Research Foundation, as indicated in the accompanying Statement of Common Ownership. Accordingly, Applicants respectfully submit that the '771 patent is not prior art.

It is believed that the double patenting rejections have been overcome. Reconsideration and withdrawal are requested.

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REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks, amendments and sequence listing, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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